

#### FIG. 1A-1

							F	.16	<b>J</b> .	1 /	<b>\-</b>									
1	ATG	GAG	TCG	GGG	CTG	CTG	CGC	CCG	GCG	CCG	GTG	AGC	GAC	GTC	ATO	GTO	· CTC	דמרו	מת'	AAC
	M	E	S.	G	L	L	R	P	A	P	V	S	Ε	V	I	۷	L	Н	Y	N
61	<b>Δ</b> Τ .	ር <sub></sub> ልር	רכה	מ מר)	ССТ	rccc	ברכר	ድድርር	ccc	יריים	CCN	ccc	rccc	יתר <i>ר</i>			20.00			.CGCC
01	v	m	ر د		, OC 1	CCG		2100	.000	CIM	CCA	<i>JJ</i> 20.		700	. د د د	וללו	GCC	iCGC	CGA	.CGCC
	1	1	G	κ.	ħ	ĸ	G	A	R	Y.	Q	Р	G	A	G	L	R	A	D	A
121	GT	GGT	GTG	CCT	GGC	GGT	GTO	CGC	CTT	CAT	CGT	GCT	'AGA	\GA4	TCT	`AGC	CGI	GTT	GTT	GGTG
	V	V	С	L	A	V	С	. <b>A</b>	F	Ι	<b>V</b>	L	E	N	L	<b>.</b> A	V	L	L	V
181	СТ	CGG.	ACG	CCA	CCC	GCG	СТТ	CCA	.CGC	TCC	CAT	GTT	CCI	GCT	CCT	`GGG	CAG	ССТ	'ראר	GTTG
	L	G	R	Н	P	R	F	Н	A	P	M	F.	L	L	L	G	S	. L	T	L
241	TC	GGA'	ГСТ	GCT	GGC	AGG	CGC	CGC	СТА	CGC	CGC	CAA	CAT	CCT	'ACT	'GTC	:GGG	GCC	GCT	CACG
	S	D	L	L	Α	G	A	Α	Y	Α	A	N	Ι	ĻL	L	S	G	P	L	T
301	CTO	GAA	ACT	GTC	ĊCC	CGC	GCT	CTG	GTT	CGC.	ACG	GGA	GGG	AGG	CGT	CTT	CGT	GGC	ACT	CACT
	L	K	L	S	Р	A	L	W	F	A	R	E	G	G	V	F	V	A	L	Т
361	GC	GTC(	CGT	GCT(	GAG	CCT	CCT	GGC	CAT	CGC	GCT	GGA	GCG	CAG	CCT	CAC	CAT	GGC	GCG	CAGG
	A	S	V	L	S	L	L	A	Ι	A	L	Е	R	S	L	T	M	Α	R	R
421	GG	GCC(	CGC	GCC(	CGT	CTC	CAG	TCG	GGG	GCG	CAC	GCT(	GGC	GÄT	GGC	ልርር	CCC	ccc	ርፕርረ	GGGC
	G	P	À	p	Ÿ	S	S	R	G	R	T	L	A	M	A	A	A	A	W W	G
403					•							•								
18T	GT(	JTC(	JCT(	GCT(	CCT	CGG	GCT	CCT	GCC.	AGC	GCT(	GGG(	CTG	GAA'	TTG	CCT	GGG'	TCG	CCT	GGAC
	V	S	L	L	L	G	L	L	P	A	L	G	W	N	С	L	·G	R	L	D
541	GC7	rtgo	CTC	CAC	rgto	CTT(	GCC	GCT	CTA	CGC	CAAC	GGC	CTA	CGT	GCT	ርጥጥ	CTC	ጉርጥ	<u>ገርጥ</u> (	CGCC
	Α	С	S	T	V	L	P	L	Y	Α	K	A	Y	V	L	F	ر د در	V	JC I ( T.	א

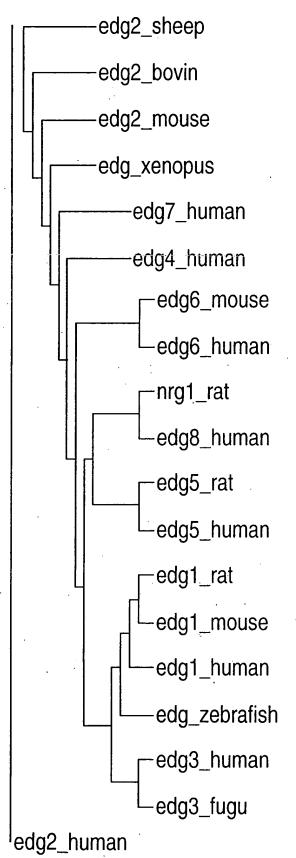


#### FIG. 1A-2

601	TT	'CGT	GGG	CAT	CCI	'GGC	CGC	TAT	CTC	TGC	CACT	CTA	ACGC	:GCG	CAT	CTA	CTG	CCA	GGT	'ACGC
	F	V	G	Ι	. <b>L</b>	A	A	Ι	С	A	L	Y	A	R	Ι	Y	С	Q	V	R
661	GC	CAA	CGC	:GCG	GCG	CCI	'GCC	:GGC	ACC	GCC	CGG	GAC	CTGC	GGG	GAC	CAC	CTC	GAC	CCG	GGCG
	A	N	Α	R	R	L	P	A	R	P	G	T	A	G	Т	T ·	S	T	R	A
721	CG	TCG	CAA	GCC	:GCG	CTC	GC1	'GGC	CTT	GCT	GCG	CAC	GCI	'CAC	CGI	GGT	GCT	ССТ	GGC	CTTT
	R																			F
781	GT	GGC	ATG	TTG	GGG	CCC	CCT	CTI	'CCI	GCI	GCT	GŤI	GCT	'CGA	CGI	'GGC	GTG	CCC	GGC	GCGC
	V		С	W							L				V			P		R
841	AC	CTG	TCC	TGT	ACT	CCT	GCA	.GGC	CGA	TCC	CTT	'CCT	GGG	ACT	GGC	CAT	GGC	CAA	CTC	ACTT
	T	С	P	V .	L	L	Q	A	D	P	F	L	G	L	A	M	A	N	S	L.
901	СТ	GAA	CCC	CAT	CAT	СТА	CAC	GCT	CAC	CAA	.CCG	CGA	CCT	GCG	CCA	.CGC	GCT	CCT	GCG	CCTG
	L		Ė																	L
961	GT	CTG	CTG	CGG	AĊG	CCA	CTC	CTG	CGG	CAG	AGA	.CCC	GAG	TGG	CTC	CCA	GCA	GTC	GGC	GAGC
	V	С	С	G	R	Н	S	С	G	R	D	P	Š	G	S	Q	Q	S	A	S
1021	GC	GGC	TGA	GGC	TTC	CGG	GGG	ССТ	GCĢ	CCG	CTG	ССТ	GCC	CCC	GGG	CCT	TGA	TGG	GAG	CTTC
	A	A	E	A	S	G	G	L	R	R	С	L	P	₽.	G		D	G·	S	F
1081	AG	CGG	СТС	GGA	GCG	СТС	ATC	GCC	CCA	GCG	CGA	CGG	GCT	ĞGA	CAC	CAG	CGG	CTC	CAC	AGGC
	S	G	S	E	R	S	S	p	Q	R	D	G	L	D	T	S	G	S	T	G
1141	AG	CCC	CGG	TGC	ACC										ACC	GGC'	TGC.	AGA	CTG	Α
	S	P	G	A	P	T	Α	Α	R	T	L	V	S	Ε	P	Α	Α	D	*	



#### FIG. 1B



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#### FIG. 1C-1

•		1										60
ede	g2_human	MAAISTSI	PV ISOPO	ETAMN	<b>FPOCFYN</b>	VEST	AFFYN	RSGKH	IAT FU	PATAL	KT VMGT	GI
ede	g7_human			MN	ECHYE	)KHM	DFFYN					
edo	4_human			MVI							KDVIVVV	
	g1_human		TS VPLVK				VRHYN'		NISA			
	3_human				LQPVRGN						S.TLTT	
	5_human				YSEYLNP		QEHYN				SROVASA	
	18_human			MECCI	IDDYDAC							
	16_human	MN A	TG TPVAP	FCCOO	LAAGGHS		A FULIAL	ICCDI	ACD CC	UPUA	GLRADAY	IVUL
cuç	yo_namun	LINV	IU ITYAF	LJUUU	LAAUUNS	ואנו	A TU I IAL	13UKL	Auk.uu	ויינוענ	GLGALRO	177
		61										100
-pdn	2_human		AN LLVMV	A T VIVA	RREHEPI	VVI	MANIA	LADEE	ACLAVE	VIME	<u>И</u> ТОВИТО	120
	7_human	FFCLFIFF					MANLA		AGLAYF	= :::	MTGPNTF	
	4_human	TVSVLVLL			RKFHFPF		LANLAA		AGIAYV		NEGPVSK	
Δdn	1_human	LICCFIIL		10	RRFHOPI				AGVAYL		HTGPRTA	
	3_human	VICSFIVI	<b></b>		KKFHPPM		IGNLAL		AGVAYT		LEGATTY	
	5_human	ILCCATVU			NKFHNRM		IGNLAL		AGIAYK		MEGKKTF	
		1 0 0			SKFHSAM				AGVAFV.		LEGSVTL	
	8_human	AVCAFIVL			PRFHAIPM		LGSLIL	SDLL	AGAAYA.	ANIL	LEGPLTL	
eug	6_human	AASCLVVLI	EN LLVLA/	41 I]2H	MRSRR <u>WV</u>	YYL I	<u> LANTIF</u>	<u> PAFF</u>	<u>I GAAY L</u>	<u>anvl</u>	<u>L</u> \$GARTF	RLA
		101										
oda	2 human	121 VSTW 1 DOF	TOTOL	LYCAY	AND A A TATE	CDAL 1	TUCN	MALIL	TOUCUD	N		<u> 180</u>
	2_human	VSTWLLRO			NLLAIAI						TWIVVIV	
	7_human	VNRWFLROK			NLLVIAV				SNLTKKI		LILLVWA	
	4_human	LEGWFLRO			TLLAIAV				SRLPRGI	1	LIVGVWV	
. •	l_human	PAQWFLREG			SLLAIAI		TMLK.		NGSNNFI	·F · -	LISACWV	
	3_human	PTVWFLREG			SLLAIAI		TMIK.		DANKRHI	T	LIGMCWL	IAF
	5_human	PVQWFAREG	· · · · · · · · · · · · · · · ·		SLLAIAI		AIAK.		GSDKSCF		LIGASWL	
	3_human	PALWFAREG		ASVL	SLLAIALE	RS L	TMAR.	RGPA 1	PVSSRGF	RITLA I	MAAAAWG'	VSL
eagt	5_human	PAQWFLREG	<u>il letala</u>	ASIF.	SLLFTAGE	ERF A	TMVRP	VAES (	GATKTSF	VYG	FIGLCWLI	LAA
	•	101					•					<del></del> ;
	<b>.</b> 1	181							<u> </u>			24.0
	2_human	VMGAIPSVG	WINCICDI	ENCS I	NMAPLYSD	)S Y L	VFWAII	FNLV 1	FVVMVV	'LYA]H	HIFGYVRO	)RT
eag/	'_human	FMGAVPTLG	WINCLCNI	SACS S	SLAPIYSR	RSIY L	VFWTVS	SNLM A	\FLIMVV	'VYL]I	SIYVYVKF	
•	_human	GLGLLPAHS	W HCLCAL	DRCS I	RMAPLLSR	ISP L	AVWALS	SSLL V	/FLLMVA	.VYT]f	RIFFYVRF	RRV
	_human	ILGGLPIMG					<b>LFCTT</b> \	/FTL L	LLSIVI		RIYSLVRI	
	_human	TLGALPILG					AFCIS1				RIYFLVKS	
	_human	VLGGLPILG				HY V	LCVVTI				IYCVVRS	
edg8	_human	LLGLLPALG	W NCLGRLI	DACS 1	TVLPLYAK	AY V	L FCVI A	FVG I	LAATCA	IYALR	TYCOVRA	NΔ
edg6	_human [	LLGMLPLLG	W]NCLCAFI	DRCS S	SLLPLYSK	RY I	LFCLVI	FAG V	LATIMG	LYGIA	IFRI VOA	SG
										<u>~ · ~</u> ) '		. <b></b> .



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#### FIG. 1C-2

	241				300
edg2_human	MRMSRHSSGI	P RRNF	R DTMMSLLKT	V VIVLGAFII	C WTPGIVIIII D VCCP OC
edg7_human	NVLSPHTSGS	S ISRF	RTPMKLMKT	V MTVLGAFVV	C WTPGLVVLLL DGLNCRQC
edg4_human	QRMAEHVSCH	ł PRYF	R ETTLSLVKT	V VIILGAEVV	C WTPGQVVLLL DGLGCESC
edg1_human		.KNISKASRS			C WAPLFILLL DV.GCKVKTC
edg3_human		.NNS			C WSPLFILFLI DV.ACRVQAC
edg5_human	ADMA	A	POTLALLKT	V TIVLGVFIV	C_WLPAFSTLLL DY_ACPVHSC
edg8_human	RRLPARPGTA	. GTTSTRARRK	PRSLALLRT	L SVVITAFVAC	C WGPIFILLLINV ACPARTO
edg6_human	QKAP	RPAARRK	ARRLLKT	/ LMILLAFLV(	C WGPLFGLLLA DVFGSNLWAQ
			•		
	301				360
edg2_human.	DVLAYEKFFL	LLAEFNSAMN	PIIYSYRDKE	E MSATFRQIL(	C CORSENPTGP TESSDRSASS
edg7_human	GVUHVKKWFL	LLALLNSVVN	PITYSYKDFI	) MYGTMKKMIA	CESOEND EDDDSD
edg4_human	NVLAVEKYFL	LLAEANSLVN	AAVYSCRDAE	MRRTFRRLLO	CACLROSTRE SVHYTSSAQG
edg1_human	DITLEKAFILE	VLAVLNSGIN	PILYILINKE	MRRAFIRIMS	S CCKCPSGD S
edg3_human	PILFKAQWFI	VLAVLNSAMN	PVIYTLASKE	MRRAFFRLV.	.CNC.LVR
edg5_human	<b>LIFIKAHA</b>	AVSILNSLLN	PVIYTWRISRD	) I RRFVI RPI O	) CWRPGVGV
edg8_human	PVLLQADIPFL	GLAMANSLLN	PIIYTLTNRD	) IRHALLRIVC	CGRHSCGRDP SGS ONSAS
edg6_human	EYLKGMD <u>WIL</u>	<u>ALAVLNSAVN</u>	<u>PIIYSFR</u> SRE	VCRAVLSFLC	CGCLRLGMRG PGDCLARAVE
	201				
adal human	361	CHDHCHH			418
edg2_human	LNHTILAGVH	SNDHSVV			
edg7_human	TA21AF2K2D	IGSUYIEUSI	SUGAVENKST	S	
edg4_human	DASIKIMLYE	NUHPLMIPPH	SYLELURYAA	SNKSTAPDDL	WVLLAQPNQQ D
edg1_human	AGKFKRPIIA		.SUNSSHPQK	DEGONPETIM	SSGNVNSSS
edg3_human	RGARASPIQP	ALDESKSKSS	22NN22H2LK	VKEDLPHTDP	SSCIMDKNAA LQNGIFCN
edg5_human	UKKKVU I PUH	HLLPLRSSSS	LEKGMHMPIS	PIFLEGNTVV	
edg8_human	ANCASTAC	CLPP DDC5	202FK22LOK	DGLDTSGSTG	SPGAPTAART LVSEPAAD
edg6_human	AHSGASTTDS	SLRP.RDSFR	P2K2F2FKWK	FLF22122AK	\$1

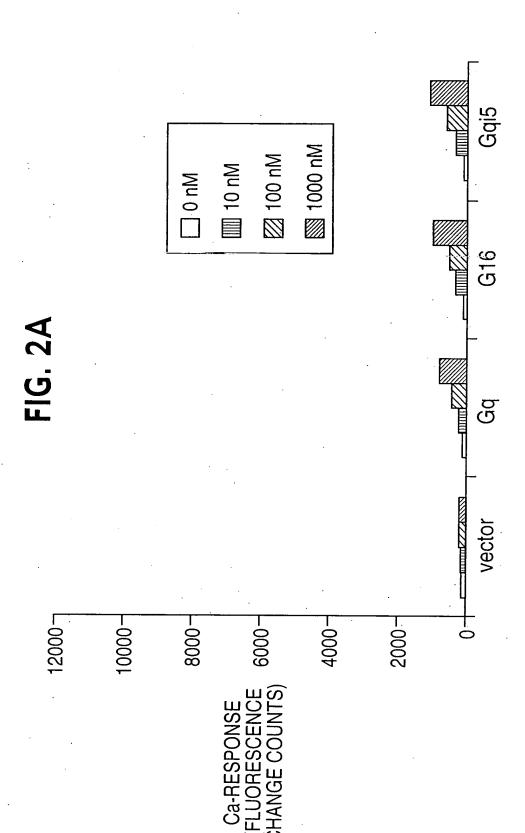
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1.







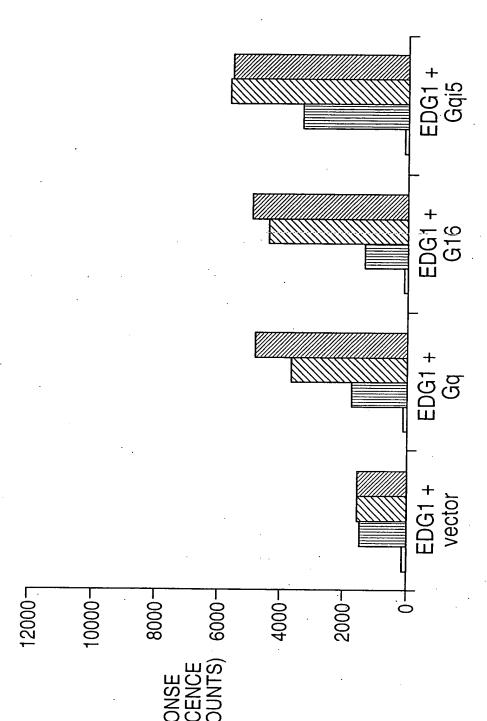
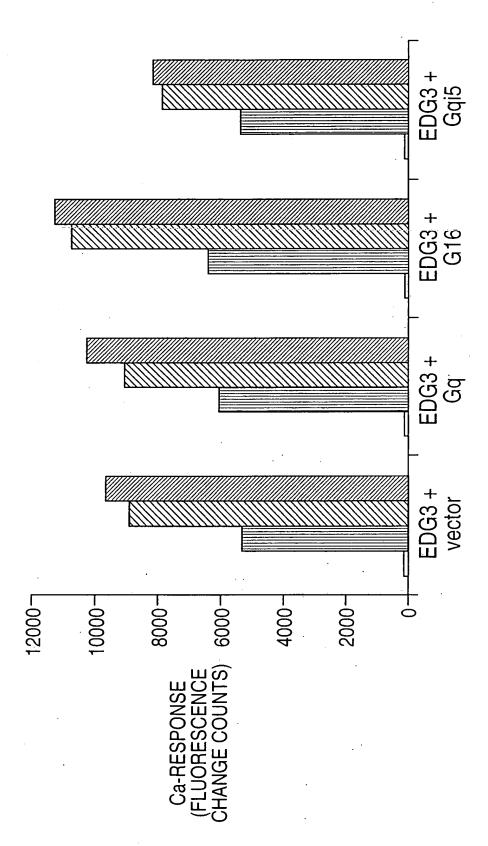


FIG. 2B











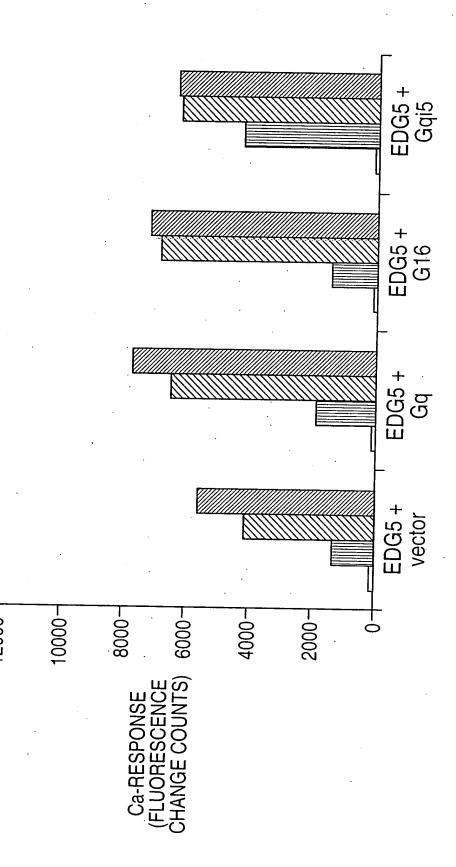
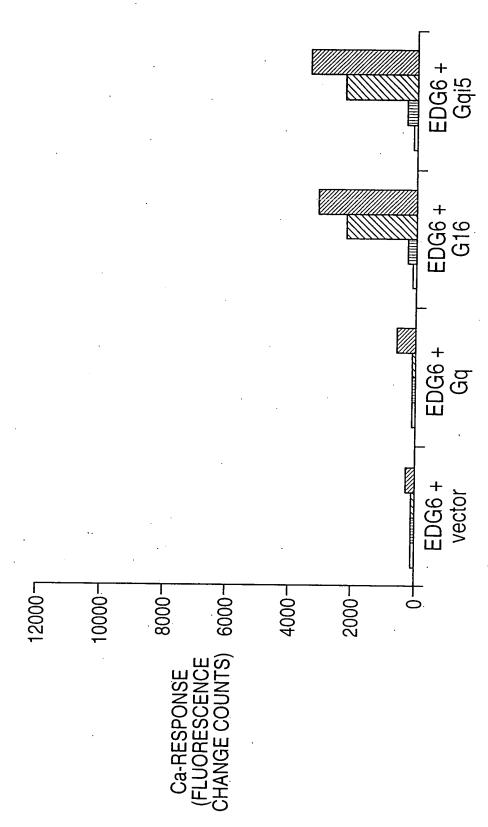
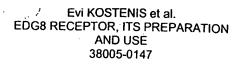




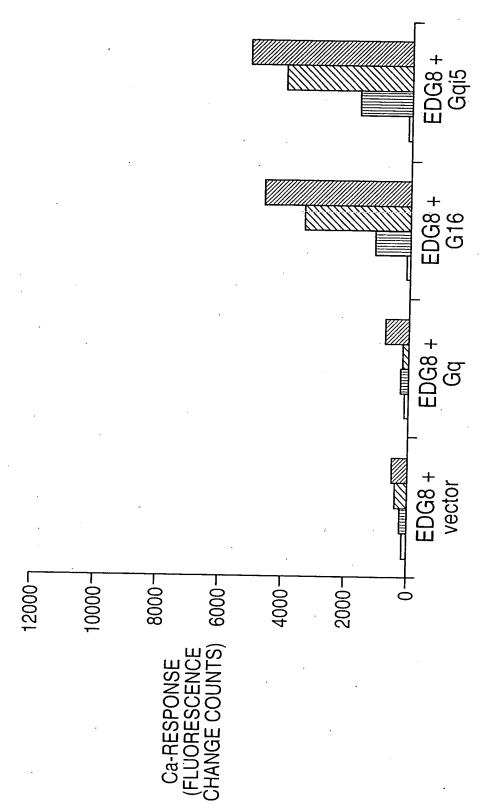
FIG. 2E





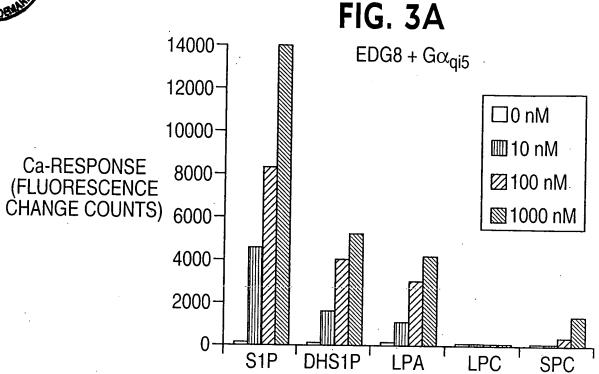


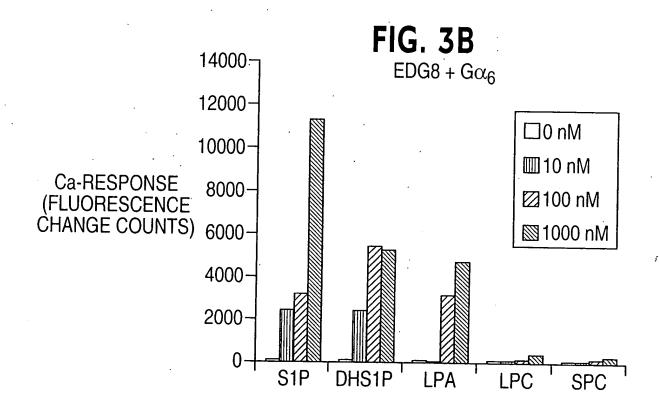


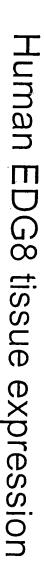


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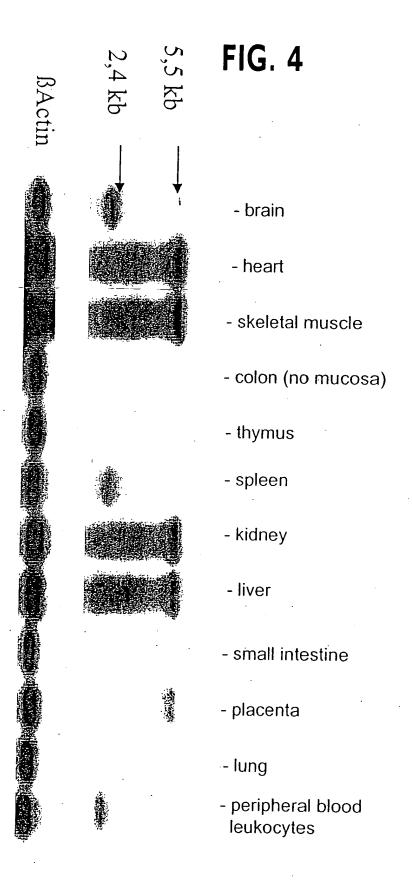
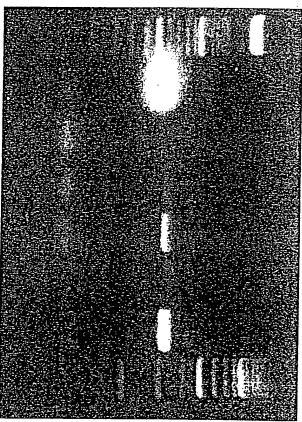


FIG. 5A

522 bp



Pos. control
neg. control
HUVECS
HMVECL
HPAEC

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FIG. 5B



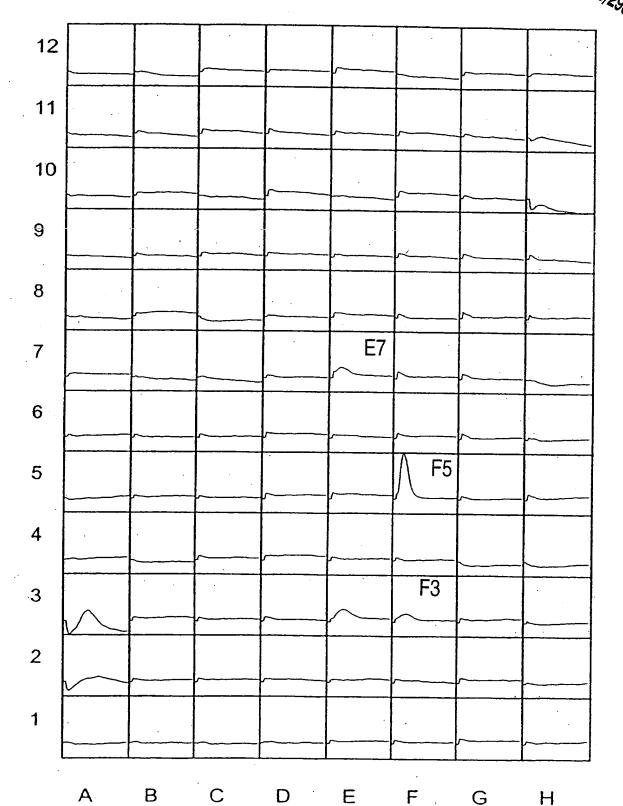
EDG-123456780



FIG. 6A qi5 background

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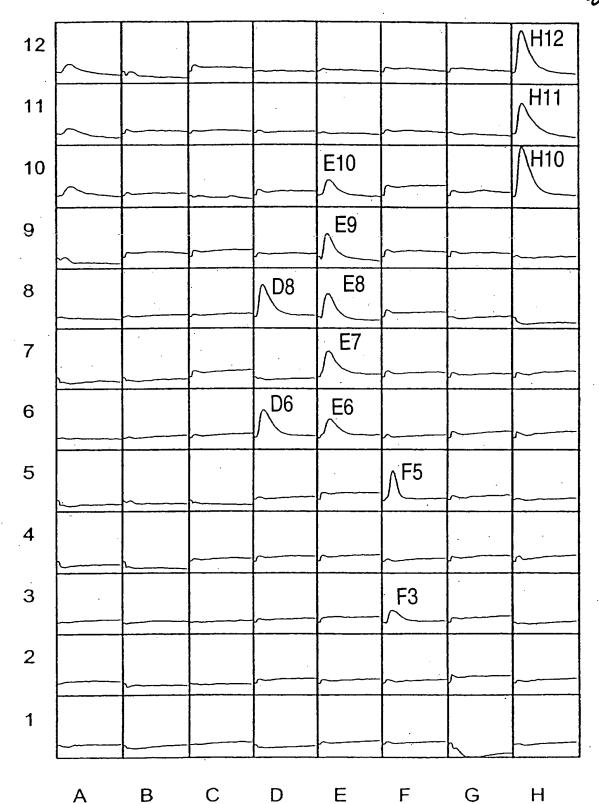
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## FIG. 6B rEDG8





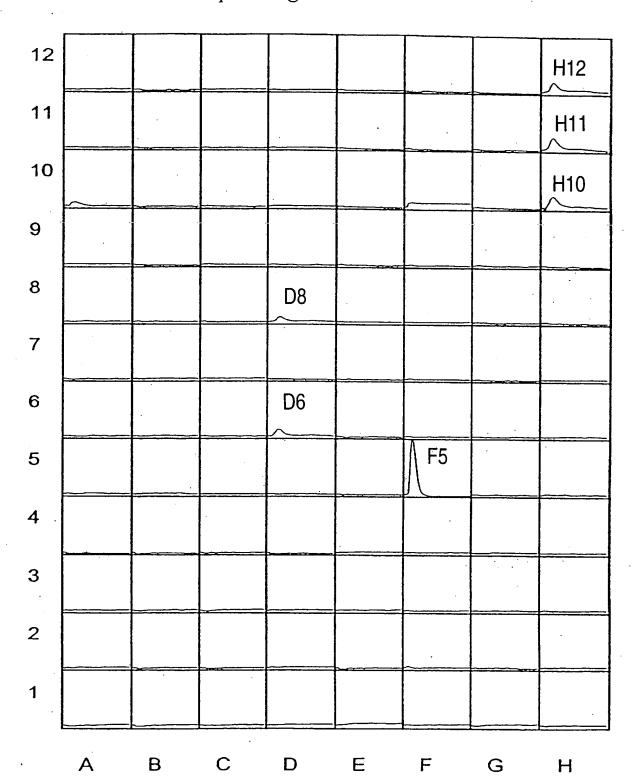


## **FIG. 6C** Tuorescence Change co

Wells	Lipid	background	rEDG8	stand. response
H10-H12	1µM S1P	0	5196	5196
	1µM LPA	5893	4327	-1566
F3	1µM cPAF	1017	1570	553
E10	1µM EPA PAF	0	1354	1354
E3	1µM AA PAF	0	3121	3121
臣8	1µM Enantio PAF	0	3883	3883
E7	1µM paf C18:1	1256	3765	2509
E6	1µM Lyso PAF	0	2421	2421
D8	1µM dhS1P	0	5144	5144
D6	1µM S1P	0	3672	3672



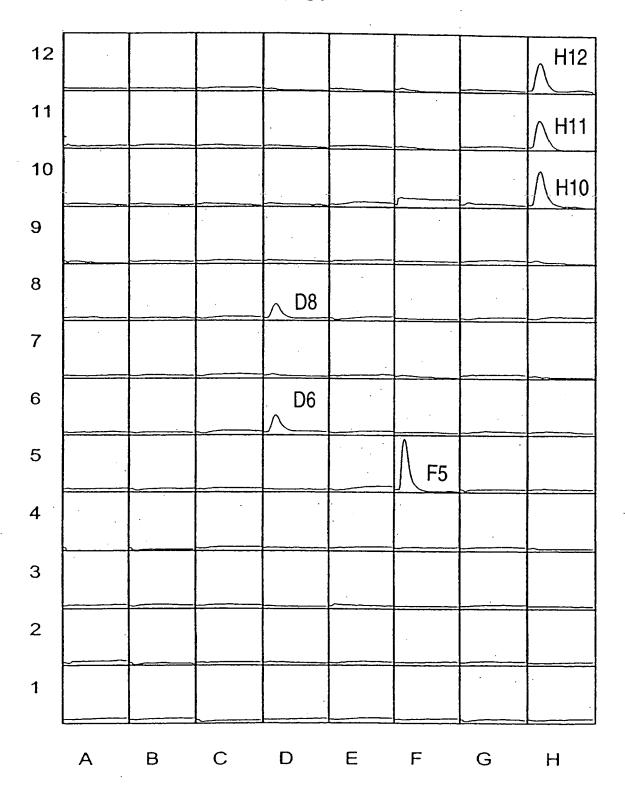
**FIG. 7A** qi5 background in HEK





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## FIG. 7B hEDG8





# Flg. 7C Fluorescence change counts

Wells	Lipid	background	hEDG8	stand. response
H10-H12	1µM S1P	9698	9493	2625
F5	1µM LPA	18004	16333	-1671
28	1µM dhS1P	1683	4522	2839
90	1µM S1P	2273	5005	3332



